86. An apparatus as described in Claim 80 wherein the incubating mechanism has wells which hold corresponding cells and wherein the robotic mechanism includes a pipette which transfers media from individual cells to the determining mechanism at predetermined intervals.

87. An apparatus as described in Claim 80 wherein the robotic mechanism dispenses 1 to 95 microliters of media.

88. An apparatus as described in Claim 80 including a liquid handling system connected to the robotic mechanism and a mechanism for cleaning of the liquid handling system with wash cycles.

89. An apparatus as described in Claim 86 including P additional pipettes in communication with the wells, each pipette can either aspirate or dispense liquid to the wells, where P is an integer greater than or equal to 2.

90. An apparatus as described in Claim 86 including a syringe pump connected to the pipette to aspirate or dispense liquid through the pipette.

91. Apparatus as described in Claim 90 wherein the syringe pump includes a 250 microliter syringe pump.

desired condition and in which the plurality of cells can be individually examined while the environment is dynamically controlled and maintained in the desired condition; and

a mechanism for determining the state of the cells, said determining mechanism in communication with the incubating mechanism, said determining mechanism includes an imaging mechanism which individually images each cell of the plurality of cells in the incubating mechanism.

Please cancel Claims 2-40 and 46.

Please add the following claims.

47. An apparatus as described in Claim 1 wherein the imaging mechanism includes a mechanism for phase contrast imaging to identify the state of each cell.

48. An apparatus as described in Claim 47 wherein the phase contrast imaging compares images to each other serially to identify the state of the cells.

49. An apparatus as described in Claim 1 wherein the imaging mechanism acquires two successive fluorescent images of each cell and compares them to each other serially to identify the state of each cell.

50. An apparatus as described in Claim 1 wherein the imaging mechanism includes antibody type labels with different colors of dyes for use to detect the presence of cell surface markers.

51. An apparatus for incubating and determining the state of cells comprising:

a mechanism for incubating cells having a dynamically controlled environment in which the cells are grown, which is maintained in a desired condition and in which individual cells can be examined in real time over time while the environment is dynamically controlled and maintained in the desired condition; and

a mechanism for determining the state of the individual cells in real time over time, said determining mechanism in communication with the incubating mechanism.

52. An apparatus as described in Claim 51 wherein the determining mechanism includes a mechanism for determining a biological event in the cell.

53. An apparatus as described in Claim 52 wherein the determining mechanism includes a mechanism for determining when a cell has doubled.

54. An apparatus as described in Claim 53 wherein the determining mechanism includes a mechanism for determining what stage a cell is in with respect to doubling.

55. An apparatus as described in Claim 54 wherein the determining mechanism includes a mechanism for determining the stage of the cell based on a metabolic process the cell is experiencing.

56. An apparatus as described in Claim 55 wherein the determining mechanism identifies the production or degration of proteins, simple or complex sugars, individual amino acids, individual ions, or individual molecules with respect to both physical presence and biological activity of the cell.

57. An apparatus for growing cells comprising:

a mechanism for incubating cells having a dynamically controlled environment in which the cells are grown, which is maintained in a desired condition and in which cells can be examined while the environment is dynamically controlled and maintained in the desired condition; and

a mechanism for tracking and identifying division and differentiation of individual cells over time.

58. An apparatus as described in Claim 57 wherein the incubating mechanism includes a first well in which a first cell is disposed and a second well in which a second cell is disposed, and including a mechanism for controlling the division and differentiation of the first cell and the second cell while the cells are in the incubating mechanism.

59. An apparatus as described in Claim 58 wherein the controlling mechanism controls the division and differentiation of the first cell differently from the way it controls the division and differentiation of the second cell while the cells are in the incubating mechanism.

60. An apparatus as described in Claim 59 wherein the first cell is a different type of cell then the second cell.

61. An apparatus as described in Claim 60 wherein the controlling mechanism includes a mechanism for limiting differentiation of the daughter cells of the first cell.

62. An apparatus has described in Claim 61 wherein the identifying mechanism includes a mechanism for assessing synergistic or antagonistic effects of different combinations of factors on the cells.

63. An apparatus as described in Claim 62 wherein the identifying mechanism includes a mechanism for identifying kinetic data for rates of cell division and differentiation.

64. An apparatus as described in Claim 63 wherein the controlling mechanism controls the cell with transcriptional regulators and regulators associated with adherence in cell differences based on time.

65. An apparatus for developing desired processes for control of a cell comprising:

a mechanism for incubating a plurality of cells having a dynamically controlled environment in which the cells are grown, which is maintained in a desired condition and in which cells can be examined while the environment is dynamically controlled and maintained in the desired condition;

a robotic mechanism including a robotic arm for dispensing and aspirating different material to each cell of the plurality of cells; and

a mechanism for determining which materials enhance the desired process in regard to each cell of the plurality of cells.

66. An apparatus as described in Claim 65 wherein the robotic mechanism varies the environment between a static environment and a dynamically changing environment.

67. An apparatus as described in Claim 66 wherein the incubating mechanism includes a first well and a second well in which a first cell and a second cell are disposed, respectively, and wherein the determining mechanism includes a diagnostic mechanism in communication with the robotic mechanism for ascertaining the occurrence of a pre-determined biological event in the first and second wells.

68. An apparatus as described in Claim 67 wherein the biological event includes growth, differentiation, expression or the secretion of a protein or hormone.

69. An apparatus as described in Claim 68 wherein the robotic mechanism automatically dispenses or aspirates media to the first and second wells.

70. An apparatus for growing cells comprising:

a mechanism for incubating a first cell and at least a second cell having a dynamically controlled environment in which the first cell and at least the second cell are grown, which is maintained in a desired condition and in which the first cell and at least the second cell can be examined while the environment is dynamically controlled and maintained in the desired condition;

a mechanism for individually controlling the division and differentiation of the first cell and at least the second cell while the cells are in the incubating mechanism, said controlling mechanism controls the division and differentiation of the first cell differently from the way it controls the division and differentiation of the second cell while the cells are in the incubating mechanism; and

a mechanism for individually tracking and identifying division and differentiation of the first cell and at least the second cell over time.

71. A method for growing cells comprising the steps of:

incubating a first cell and at least a second cell in a dynamically controlled environment in which the first cell and at least the second cell are grown, which is maintained in a desired condition and in which the first cell and at least the second cell can be examined while the environment is dynamically controlled and maintained in the desired condition; and

controlling the division and differentiation individually of the first cell and at least the second cell while the cells are in the controlled environment.

72. A method as described in Claim 71 wherein the controlling step includes the step of controlling the division and differentiation of the first cell differently from the way

the division and differentiation of the second cell are controlled while the first cell and the second cell are in the controlled environment.

73. A method for developing desired processes for controlling cells comprising the steps of:

incubating a plurality of cells in a dynamically controlled environment in which the cells are grown, which is maintained in a desired condition and in which the cells can be examined while the environment is dynamically controlled and maintained in the desired condition;

dispensing and aspirating different material to each cell with a robotic arm of a robotic mechanism; and

determining which materials enhance the desired processes in regard to each cell of the plurality of cells.

74. An apparatus for holding a stem cell comprising:

a mechanism for incubating the cell;

a mechanism for determining a desired state of the cell connected to the incubating mechanism; and

a mechanism for introducing quiescence media to the cell in the incubating mechanism when the cell is in the desired state to inhibit the proliferation or selected differentiation of the cell, said introducing mechanism connected to the incubating mechanism.

75. An apparatus for holding a plurality of cells comprising:

a mechanism for incubating the plurality of cells having a dynamically controlled environment in which the plurality of cells are grown, which is maintained in a desired condition and in which the plurality of cells can be individually examined while the environment is dynamically controlled and maintained in the desired condition, said incubating mechanism having a mechanism for controlling the environment about each cell in the incubating mechanism to maintain the environment about each cell in a desired condition; and

a mechanism for determining the state of the cells, said determining mechanism in communication with the incubating mechanism.

76. An apparatus as described in Claim 75 wherein the controlling mechanism includes a mechanism for exchanging n media, where n is greater than or equal to 2, in the incubating mechanism.

77. An apparatus as described in Claim 76 wherein the incubating mechanism includes m wells, where m is greater than or equal to 2, and the cell is disposed in a first of the m wells, and the exchanging mechanism exchanges n media in the first well.

78. An apparatus as described in Claim 76 wherein n equals 96.

79. An apparatus as described in Claim 75 including a mechanism for automatically testing for predetermined biological variables and engineered genes with respect to each cell.

80. An apparatus for holding cells comprising:

a mechanism for incubating the cells; and

a robotic mechanism including a robotic arm for dispensing and aspirating different material, a mechanism for controlling the environment about each cell in the

incubating mechanism to maintain the environment about each cell in a desired condition, to each cell of the plurality of cells.

81. An apparatus as described in Claim 80 including a supply of antigen and a supply of fluorochrome connected to the robotic mechanism so antigen or fluorochrome can be dispensed to the cells in the incubating mechanism.

82. An apparatus as described in Claim 65 wherein the determining mechanism determines how to insert transgenes to produce recombinant molecules.

83. An apparatus as described in Claim 65 wherein the determining mechanism determines synergistic or antagonites affects of different combinations of factors on the cellular proliferation function or other matrix.

84. An apparatus as described in Claim 65 wherein the imaging mechanism has a field and adjusts the position of the field to allow for cell movement while centering the cell in the field.

85. A method as described in Claim 71 wherein the first cell is a glioblastoma cell.

92. An apparatus as described in Claim 80 wherein the robotic mechanism includes a probe which, when placed in a well, identifies how much fluid is in the well.

93. An apparatus as described in Claim 86 wherein the pipette can remove tissue culture media, nutrients or proteins from a well.

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94. An apparatus as described in Claim 1 wherein the imaging mechanism counts the number of cells in each well.

95. An apparatus as described in Claim 80 wherein the determining mechanism analyzes tissue culture media in a well with either biochemical, immuno chemical, biological or chemical assays.

96. An apparatus as described in Claim 1 wherein the imaging mechanism uses pattern recognition to correlate a state of a cell with a particular metabolic process of the cell.

97. An apparatus as described in Claim 80 including a determining mechanism for testing for production or degradation of proteins, simple or complex sugars, individual amino acids, individual member ions than, individual molecules with respect to both physical presence and biological activity in the incubating mechanism, said determining mechanism connected with the incubating mechanism.

98. A method as described in Claim 73 wherein the cells are either single invertebrate cells, single vertebrate cells, single parasite organism, protozoan, bacterium, trypanosome, amoeba, fungus, muscle cells, fertilized ovum, glandular cells, endothelial cells, immunoreactive cells, T-cells, B-cells, Nk-cells, macrophage, neutrophil, basophil, mast-cells, eosinophil, hematopoeitic stem cells, keratinocyte cells, neuron cells, neural cells, glial cells, mesenchymal cells or mesenchymal stem cells, skin cells, embryonal stem cells, cells from a member of the phylum angiospermae (dicotyledoneae, monocotyledmeael), cells from a member of the phylum embryophyta (gymnospermae, filicineae, hepaticae, lycopodmeae, equisetineae), cells from a member of the class chlorophyta (green algae).

99. An apparatus as described in Claim 86 wherein operation of the pipette is optimized when the fluid forces applied to the cells is minimized by retaining sufficient to flow.

100. An apparatus as described in Claim 80 including a determining mechanism for obtaining kinetic data for the rates of cell division differentiation, said determining mechanism connected to the incubating mechanism.

101. An apparatus as described in Claim 65 wherein the determining mechanism identifies trends and parameters corresponding with a time before doubling of the cell.

102. A method as described in Claim 41 including after the gathering step, there is the step up purifying human hematopoeitic stem cells.

103. An apparatus as described in Claim 1 wherein the imaging mechanism recognizes when a cell doubles in the incubating mechanism by pattern recognition.

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104. An apparatus as described in Claim 1 wherein the determining mechanism includes a plurality of dyes, each dye associated with a different cell surface marker, to identify cell surface markers on a cell.

105. A method as described in Claim 71 wherein the controlling step includes the step of maintaining the first cell in a quiescent state by disposing the first cell in a quiescence media.

106. A method as described in Claim 105 including after the maintaining step, there is the step of introducing growth media to the first cell after a predetermined time the first cell is in a quiescent state.

107. An apparatus as described in Claim 65 wherein the determining mechanism records cellular events in time while the robotic mechanism manipulates the environment about the cell.

108. An apparatus as described in Claim 107 wherein the determining mechanism records information relevant to direct growth of a cell or diagnose phenotypic outcome of a division of a cell.

109. A method as described in Claim 105 wherein the maintaining step includes the step of timing how long the cell is in the quiescence media to determine whether the cell can recover and is able to start further growth.

110. An apparatus as described in Claim 65 wherein the determining mechanism screens different medias for what keeps the cells alive or dividing and then causes the robotic mechanism to add different types of serum to see what would supplement the growth of the cells.

111. An apparatus as described in Claim 34 wherein the determining mechanism determines phenotype regarding the first cell.

112. A method as described in Claim 41 wherein the growth media is either IL-11, IL-6, IL-1, HG, G-CSF or Basic FGF.

113. A method as described in Claim 41 wherein the stem cell has a phenotype demonstrated by fluorescence antibody binding which is positive for CD34+ and negative for the lineage markers having CD38 and is either Thy1+ or Thy1-.

114. An apparatus for culturing and analyzing cells, the apparatus comprising:

a biochamber having a plurality of cell housing containers in which cells to be cultured may be introduced therein;

a liquid handling system for providing exchange of media to the cells, the liquid handling system in fluid communication with the plurality of cell housing containers;

an image recognition system for analyzing the cells, the image recognition system utilizing image recognition software;

a stage for supporting the biochamber, the biochamber, liquid handling system and image recognition system being in movable registration with respect to one another whereby the liquid handling system and image recognition system can access different cell housing containers; and

a system controller capable of regulating interaction between the biochamber, liquid handling system, image recognition system and stage.

115. The apparatus for culturing and analyzing cells according to Claim 114, wherein the image recognition system further includes a microscope comprising a camera for deriving images from the cells within the plurality of cell housing containers.

116. The apparatus for culturing and analyzing cells according to Claim 115, wherein the derived images are processed by the image recognition software to determine cellular characteristics of the cells.

117. The apparatus for culturing and analyzing cells according to Claim 116, wherein upon determination of particular cellular characteristics of the cells, the system controller is prompted to actuate the liquid handling system to provide exchange of media to the cells.

118. The apparatus for culturing and analyzing cells according to Claim 114, wherein the liquid handling system aspirates, irrigates and dispenses the media to the cells.

119. The apparatus for culturing and analyzing cells according to Claim 114, wherein the liquid handling system further includes a plurality of pipettes for providing the

exchange of media to the cells, the plurality of pipettes being movable along X, Y and Z dimensions with respect to the plurality of cell housing containers.

120. The apparatus for culturing and analyzing cells according to Claim 114, wherein the stage displaces at least one of the plurality of cell housing containers with respect to the liquid handling system and the image recognition system.

121. The apparatus for culturing and analyzing cells according to Claim 114, wherein the image recognition system is capable of determining varying cellular characteristics and the system controller regulates the biochamber and liquid handling system in response to the determined cellular characteristics.

122. The apparatus for culturing and analyzing cells according to Claim 114, wherein the biochamber is respectively displaceable to both the liquid handling system and the image recognition system.

123. The apparatus for culturing and analyzing cells according to Claim 114, wherein the biochamber is displaceable along X and Y lateral dimensions and the liquid handling system and image recognition system are displaceable along a Z dimension.

REMARKS

This is a divisional application of U.S. patent application 08/741,628.

Claims 1, 41-45 and 47-123 are currently active.

Claims 2-40 and 46 have been canceled.

Claim 1 has been amended.

Claims 47-113 have been added.

Antecedent support for Claim 1 is found on page 12, line 23.

Antecedent support for Claim 47 is found on page 17, line 11.

Antecedent support for Claim 48 is found on page 42, lines 17-20.

Antecedent support for Claim 49 is found on page 42, line 30.

Antecedent support for Claim 50 is found on page 43, lines 23-34.

Antecedent support for Claim 52 is found on page 33, line 12-page 34, line 6.

Antecedent support for Claim 53 is from on page 33, line 12-page 34, line 6.

Antecedent support for Claim 54 is from on page 33, line 12-page 34, line 6.

Antecedent support for Claim 55 is found on page 30, lines 3-9.

Antecedent support for Claim 56 is from on page 30, lines 10-14.

Antecedent support for Claim 57 is found in Claim 1 and on page 33, line 12-page 34, line 6.

Antecedent support for Claim 58 is found on page 46, lines 11-20.

Antecedent support for Claim 59 is found on page 52, lines 1-22.

Antecedent support for Claim 60 is found on page 14, line 15-page 15, line 10.

Antecedent support for Claim 61 is found on page 49 and page 16.

Antecedent support for Claim 62 is found on page 30, lines 3-9.

Antecedent support for Claim 63 is found on page 32, lines 25-26.

Antecedent support for Claim 64 is found on page 51, lines 21-23.

Antecedent support for Claim 65 is found in Claim 1, page 14, lines 3-10 and page 30, lines 6-9.

Antecedent support for Claim 66 is found on page 16, lines 5-6.

Antecedent support for Claim 67 is found on page 14, lines 8-10.

Antecedent support for Claim 68 is found on page 27, line 23 and line 29.

Antecedent support for Claim 69 is found on page 14, lines 4-5.

Antecedent support for Claim 70 is found in Claim 1 and on page 12, lines 23-27.

Antecedent support for Claim 71 is found on page 23, lines 16-20 and page 52, line 7-22.

Antecedent support for Claim 72 is found on page 23, lines 16-20 and page 52, line 7-22.

Antecedent support for Claim 73 is found on page 23, lines 16-20 and page 52, line 7-22.

Antecedent support for Claim 74 is found on page 4, lines 12-14.

Antecedent support for Claim 75 is found in figure 1.

Antecedent support for Claim 76 is found on page 6, lines 20-30.

Antecedent support for Claim 77 is found on page 6, lines 20-30.

Antecedent support for Claim 78 is found on page 18, line 5.

Antecedent support for Claim 79 is found on page 9, lines 9-15.

Antecedent support for Claim 80 is found on page 14, lines 8-10.

Antecedent support for Claim 81 is found on page 8, lines 24-28.

Antecedent support for Claim 82 is found on page 15, lines 19-20.

Antecedent support for Claim 83 is found on page 16, lines 14-18.

Antecedent support for Claim 84 is found on page 22, lines 5-6.

Antecedent support for Claim 85 is found on page 23, lines 1-3.

Antecedent support for Claim 86 is found page 24, lines 10-14.

Antecedent support for Claim 87 is found on page 24, lines 18-19.

Antecedent support for Claim 88 is found on page 24, lines 25-29; page 26, lines 27-31 and page 31, lines 11-13.

Antecedent support for Claim 89 is found on page 26, lines 19-20.

Antecedent support for Claim 90 is found on page 24, line 29-30.

Antecedent support for Claim 91 is found on page 24, lines 29-30.

Antecedent support for Claim 92 is found on page 25, lines 29-30.

Antecedent support for Claim 93 is found on page 27, lines 21-24.

Antecedent support for Claim 94 is found on page 27, lines 24-26.

Antecedent support for Claim 95 is found on page 27, lines 22-31; page 28, page 29 and page 30, lines 1-2.

Antecedent support for Claim 96 is found on page 30, line 6-9.

Antecedent support for Claim 97 is found on lines 10-14.

Antecedent support for Claim 98 is found on pages 14 and 15.

Antecedent support for Claim 99 is found on page 31, lines 22-23.

Antecedent support for Claim 100 is found on page 32, lines 25-26.

Antecedent support for Claim 101 is found on page 33, lines 1-9.

Antecedent support for Claim 102 is found on pages 34, lines 14-16.

Antecedent support for Claim 103 is found on page 39, lines 14-15.

Antecedent support for Claim 104 is found on page 44, line 5-8.

Antecedent support for Claim 105 is found on page 45, lines 25-27.

Antecedent support for Claim 106 is found on page 46, lines 6-10.

Antecedent support for Claim 107 is found on page 50, lines 1-8.

Antecedent support for Claim 108 is found on page 50, lines 1-8.

Antecedent support for Claim 109 is found on page 53, lines 2-3.

Antecedent support for Claim 110 is found on page 52, lines 14-19.

Antecedent support for Claim 111 is found on page 31, lines 22-23.

Antecedent support for Claim 112 is found on page 38, lines 2-3.

Antecedent support for Claim 113 is found on page 38, lines 10-12.

Antecedent support for Claim 114 is found on page 12, lines 6 through page 14, line 10.

Antecedent support for Claim 115 is found on page 12, lines 30 and 31.

Antecedent support for Claim 116 is found on page 39, lines 26-28.

Antecedent support for Claim 117 is found on page 14, lines 3-10.

Antecedent support for Claim 118 is found on page 14, lines 3-10.

Antecedent support for Claim 119 is found on page 26, lines 19-20 and page 31, lines 1 and 8.

Antecedent support for Claim 120 is found on page 39, lines 7-31.

Antecedent support for Claim 121 is found on page 39, lines 26-31.

Antecedent support for Claim 122 is found on page 31, lines 8-14.

Antecedent support for Claim 123 is found on page 31, lines 1 and 8.

In view of the foregoing amendments and remarks, it is respectfully requested that Claims 1, 41-45 and 47-123, now in this application be allowed.

Respectfully submitted,

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